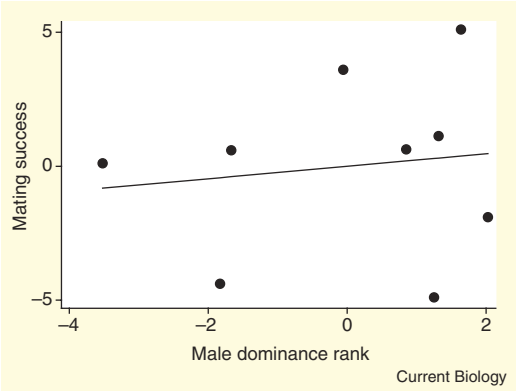

Figure 2. Effect of male dominance rank on mating success when support for alpha male is controlled statistically. Mating success was measured as the number of copulations with attractive females.

Values of mating success are based on residual values derived from the regression model.

These data suggest that cooperative tactics among male chimpanzees are as important as rank competition in determining male mating success. The alpha male at Kanyawara had much higher mating success than other males, but still allowed his allies preferential access to mates. This strategy probably extended his tenure by retaining allies who consistently supported him. For the alpha male, these lost mating opportunities may be the price of power. For his allies, the benefits derived from supporting the alpha male may be more important than achieving high status.

Supplemental data

Supplemental data including experimental procedures are available at http://www.current-biology.com/cgi/content/full/17/15/R586/DC1

Acknowledgements

Support for this study came from grants provided to K. Duffy by the UCLA Department of Anthropology, Primate Conservation, Inc., Leakey Foundation, Wenner-Gren Foundation, and a dissertation improvement grant from the National Science Foundation (BCS-0089921) awarded to J.B. Silk and K.G. Duffy. The Kibale Chimpanzee Project received support from grants provided to R.W. Wrangham by the National Science Foundation (BCS-0416125) and by the Leakey Foundation. We wish to thank the Makerere University Biological Field Station (MUBFS), the Ugandan National Council for Science and Technology, and the Uganda Wildlife Authority for allowing us to work in Kibale National Park. We also thank the late John Barwogeza, the late Muhangyi Donor, Christopher Katongole, Francis Mugurusi, the late Christopher Mururuli, and Peter Tuhairwe for their invaluable assistance in collecting data and following chimpanzees. Thanks also go to the field manager, Katharin Pieta for logistical assistance. We appreciate comments made on an earlier version of this manuscript by Karline Janmaat. We thank Bill McGrew for useful comments on the manuscript.

References

1. Mitani, J.C., Merriwether, D.A., and Zhang, C. (2000). Male affiliation, cooperation and kinship in wild chimpanzees. Anim. Behav. *59*, 885–893.
2. de Waal, F.B.M. (1984). Sex differences in the formation of coalitions among chimpanzees. Ethol. Sociobiol. *5*, 239–255.
3. Nishida, T. and Hosaka, K. (1996). Coalition strategies among adult male chimpanzees of the Mahale Mountains, Tanzania. In Great Ape Societies, W.C. McGrew, L.F. Marchant, and T. Nishida, eds. (Cambridge: Cambridge Press), pp.114–134.
4. Constable, J.L., Ashley, M.V., Goodall, J., and Pusey, A.E. (2001). Noninvasive paternity assignment in Gombe chimpanzees. Mol. Ecol. *10*, 1279–1300.
5. Boesch, C., Kohou, G., Nene, H., and Vigilant, L. (2006). Male competition and paternity in wild chimpanzees of the Tai Forest. Am. J. Phys. Anthropol. *130*, 103–115.
6. de Waal, F.B.M. (1982). Chimpanzee politics (London: Jonathan Cape).
7. Goodall, J. (1986). The Chimpanzees of Gombe: Patterns of Behavior (Cambridge, Massachusetts: Belknap Press).
8. Boesch, C. and Boesch-Achermann, H. (2000). The Chimpanzees of the Tai Forest: Behavioral Ecology and Evolution (Oxford: Oxford University Press).
9. Muller, M. (2002). Agonistic relations among Kanyawara chimpanzees. In Behavioural Diversity in Chimpanzees and Bonobos, C. Boesch, G. Hohmann, and L. Marchant, eds. (Cambridge: Cambridge Press), pp. 112–124.
10. Muller, M., Emery-Thompson, M. and Wrangham, R.W. (2006). Male chimpanzees prefer mating with old females. Curr. Biol. *16*, 2234–2238.

[1]Department of Anthropology, University of California at Los Angeles, 341 Haines Hall, Los Angeles, California 90095, USA. [2]Department of Anthropology, Harvard University, 11 Divinity Avenue, Cambridge, Massachusetts 02138, USA. E-mail: jsilk@anthro.ucla.edu

Modulation by dopamine of human basal ganglia involvement in feedback control of movement

Florian Kempf[1], Christof Brücke[1], Andrea A. Kühn[1,2], Gerd-Helge Schneider[3], Andreas Kupsch[1], Chiung Chu Chen[2,4], Alexandros G. Androulidakis[2], Shouyan Wang[5], Wim Vandenberghe[6], Bart Nuttin[7], Tipu Aziz[5,8] and Peter Brown[2]

We learn new motor tasks by trial and error, repeating what works best and avoiding past mistakes. To repeat what works best we must register a satisfactory outcome, and in a study [1] we showed the existence of an evoked activity in the basal ganglia that correlates with accuracy of task performance and is associated with reiteration of successful motor parameters in subsequent movements. Here we report evidence that the signaling of positive trial outcome relies on dopaminergic input to the basal ganglia, by recording from the subthalamic nucleus (STN) in patients with nigrostriatal denervation due to Parkinson's Disease (PD) who have undergone functional neurosurgery. Correlations between subthalamic evoked activities and trial accuracy were weak and behavioral performance remained poor while patients were untreated; however, both improved after the dopamine prodrug levodopa was re-introduced. The results suggest that the midbrain dopaminergic system may be important, not only in signaling explicit positive outcomes or rewards in tasks requiring choices between options [2,3], but also in trial-to-trial learning and in reinforcing the selection of optimal parameters in more automatic motor control.

We studied seven patients with PD in whom the STN was

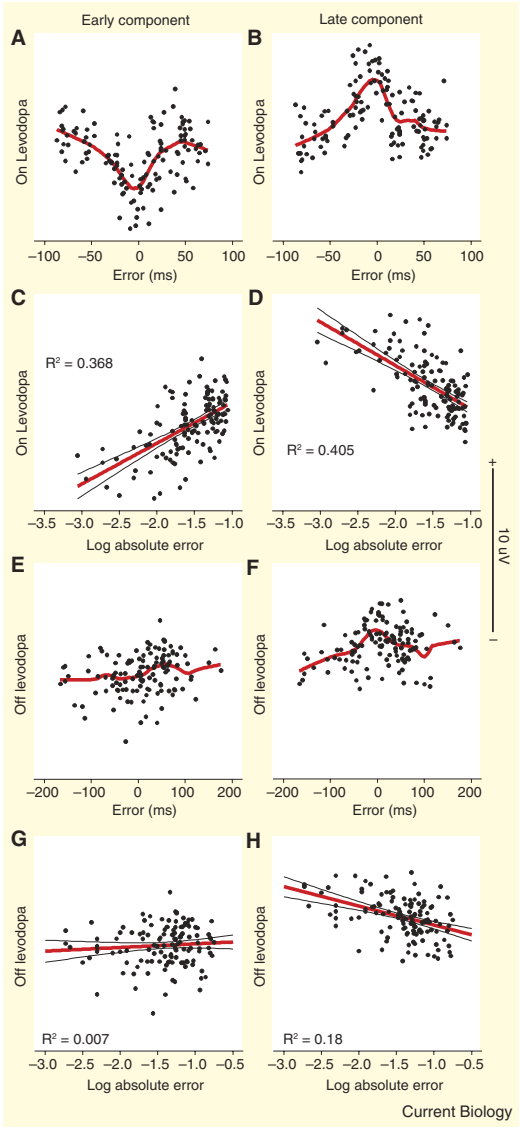

Figure 1. Example correlations between LFP activity and error.

Data are from contact pair 23 in the right STN and were recorded as the right hand stopped the spot trajectory (time zero) in case 4. (A–D) Recorded during treatment with levodopa; (E,F) recorded after overnight withdrawal of levodopa. (A) Scatter plot of trial error and amplitude of evoked activity averaged over 189–289 ms after stopping of spot on levodopa. Negative errors mean that the spot was stopped before the vertical target line was reached. The most negative evoked potentials follow trials with the least error. (B) Same for 481–581 ms after stopping spot. The most positive evoked potentials follow trials with the least error. (C) Linear regression analysis (red line) of relationship between LFP amplitude and log absolute error of data in A. Thin black lines are 95% confidence limits of regression line. (D) Same for data in B. (E) Scatter plot of trial error and amplitude of evoked activity averaged over 189–289 ms after stopping spot off levodopa (significant correlations were absent throughout the early period <320 ms). (F) Same for 413–513 ms after stopping spot. (G) Regression analysis of relationship between LFP amplitude and log absolute error of data in E. (H) Same for data in F. Scatter plots in (A,B,E,F) are fitted by Loess local regression. Correlations in (C,D,H) were significant ($p > 0.001$). Note that trial error is higher (see change in x-axis scales in (E–H)), and the dependency of evoked activity on error is diminished without treatment with levodopa.

implanted bilaterally (cases 1–6) or unilaterally (case 7) as part of ameliorative functional neurosurgery (see Table S1 in the Supplemental data available on-line with this issue). Local field potentials (LFPs) were recorded while patients engaged in a PC 'game' in which they would start the movement of a spot on the left of a computer screen by pressing a push-button held in one hand and then, as accurately as possible, stop the spot as it crossed a target line in the middle of the screen by pressing a second push-button held with the other hand. Patients were tested with and without temporary reversal of dopaminergic hypofunction by treatment with the dopamine precursor, levodopa.

We sought differences in the correlations between the error in each trial and the amplitude of the STN LFP that followed in the two treatment states. As error can be positive or negative, and as by far the biggest changes in LFP amplitude (whether positive or negative in polarity) have been previously found to occur with the smallest error [4], we took the logarithmic transform of the absolute error in each trial and correlated this with the amplitude of LFP activity. Two periods of LFP activity were considered; within 320 ms of the stopping of spot trajectory and from 320–1000 ms thereafter. We selected the best correlations per time period (see Supplemental Experimental Procedures in Supplemental data) from the three contact pairs of each implanted electrode and from the runs with the left and right hand stopping the spot trajectory per recording side in each treatment state (Figure 1).

An ANOVA of the coefficients of determination (r^2) demonstrated a main effect of drug state ($F_{[1,12]} = 16.168$, $p = 0.002$), and an interaction between time period and drug state ($F_{[1,12]} = 5.734$, $p = 0.034$). The latter was due to a greater reduction in the strength of correlation with trial error over the first compared to the second time period in the off compared to the on drug state (Figure 2A).

The accuracy of coding of trial error by neuronal population activity as reflected by LFP amplitude will depend on both the consistency and gradient in the relationship between trial error and amplitude. Accordingly, we also determined whether the weakening of the amplitude-error correlations after overnight withdrawal of levodopa entailed a reduction in the gradient of the relationship between variables, so that component amplitudes became smaller for the same degree of accuracy without levodopa treatment (compare Figure 1A–D with E and H). There was a 51% drop ($t_{[12]} = 4.213$, $p = 0.001$) in absolute gradient in the regression of early component amplitude with error upon withdrawal of levodopa (Figure 2B). However, there was no drop in absolute gradient with respect to the late component ($t_{[12]} = 0.143$, $p = 0.889$).

Thus, in the relative absence of dopamine input, there is a reduced scaling of the amplitude of the early component with trial error whereas, by exclusion, an increase in the inconsistency of this relationship likely accounts for the drop in correlation during the second time period. Note that the amplitude of averaged

evoked LFP activities measured over the same time periods as the correlations did not differ between drug states, so that the increase in inconsistency in the relationship between amplitude and error was unlikely to be due to a change in the signal-to-noise ratio of evoked activities between states (see Supplemental data). Reduced scaling of amplitude with trial error and increased inconsistency in this relationship after withdrawal of levodopa would both act to undermine the value of off-line feedback processing in the basal ganglia in determining motor parameters for the next trial, and would suggest that performance should be compromised in the untreated state. In line with this, an ANOVA of task error demonstrated a main effect of drug state ($F_{[1,6]} = 12.247$, $p = 0.013$; Figure 2C), but no effect of hand ($F_{[1,6]} = 0.363$, $p = 0.569$) nor drug state–hand interaction ($F_{[1,6]} = 0.002$, $p = 0.962$).

The basal ganglia's role in processing feedback used in the offline optimisation of motor performance is thus dependent on dopaminergic input in the human, extending the potential role of the midbrain dopaminergic system in signaling explicit reward in essentially cognitive tasks entailing the choice between movements [5,6] to an involvement in signaling positive trial outcome after execution of a single movement. Under these circumstances the dopaminergic signal may contribute to offline trial-to-trial motor learning [1], distinct from within trial error correction mechanisms and more chronic habit learning, both of which may also involve the basal ganglia [4,7]. Tonic [8] as well as phasic [1,2] dopaminergic input may be important in the population response to positive trial outcome, as pre-synaptic re-uptake mechanisms mean that both may have been improved by treatment with levodopa in our PD patients. Finally, it is interesting that we recorded our dopamine dependent positive feedback signal in STN, a key node in the indirect pathway of the basal ganglia [9], activity in which would act to disfacilitate cortex and limit possible changes in motor parameters prior to the next trial.

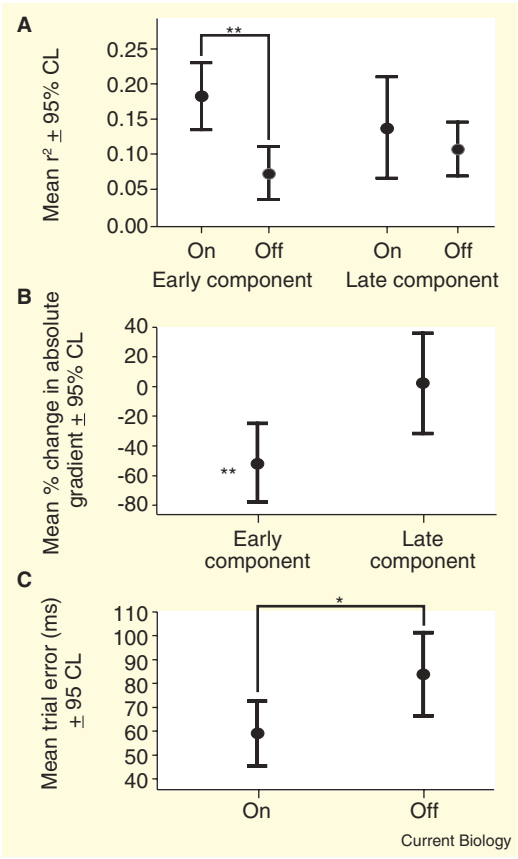

Figure 2. Group effects of withdrawal of levodopa on correlations and performance.
(A) Group mean r2 between evoked LFP amplitude and log absolute trial error on and off treatment with levodopa. (B) Group mean % change in absolute gradient of regression of LFP amplitude and log absolute trial error upon withdrawal of levodopa. Negative values represent a reduction of gradient. (C) Group mean trial errors during treatment with levodopa and following withdrawal of levodopa. ** = $p \leq 0.001$ and * = $p \leq 0.05$ (paired t-tests). CL = confidence limits.

Supplemental data

Supplemental data including experimental procedures are available at http://www.current-biology.com/cgi/content/full/17/15/R587/DC1

Acknowledgments

This work was supported by the Medical Research Council. W.V. is a Senior Clinical Investigator of the Fund for Scientific Research – Flanders.

References

1. Brown, P., Chen, C.C., Wang, S., Kühn, A.A., Doyle, L., Yarrow, K., Nuttin, B., Stein, J., and Aziz, T. (2006). Involvement of human basal ganglia in off-line feed-back control of voluntary movement. Curr. Biol. *16*, 2129–2134.
2. Schultz, W. (2002). Getting formal with dopamine and reward. Neuron *36*, 241–263.
3. Schultz, W. (2007). Behavioural dopamine signals. Trends Neurosci. *30*, 203–210.
4. Matsumoto, N., Hanakawa, T., Maki, S., Graybiel, A.M., and Kimura, M. (1999). Role of nigrostriatal dopamine system in learning to perform sequential motor tasks in a predictive manner. J. Neurophysiol. *82*, 978–998.
5. Frank, M.J., Seeberger, L., and O'Reilly, R.C. (2004). By carrot or by stick: Cognitive reinforcement learning in Parkinsonism. Science *306*, 1940–1943.
6. Shohamy, D., Myers, C.E., Onlaor, S., Grossman, S., Sage, J., Gluck, M.A., and Poldrack, R.A. (2004). Cortico-striatal contributions to feedback-based learning: Converging data from neuroimaging and neuropsychology. Brain *127*, 851–859.
7. Smith, M.A., Brandt, J., and Shadmehr, R. (2000). The motor dysfunction in Huntington's Disease begins as a disorder in error feedback control. Nature *403*, 544–549.
8. Aosaki, T. Graybiel, A.M., Kimura, M. (1994) Effect of the nigrostriatal dopamine system on acquired neural responses in the striatum of behaving monkeys. Science *265*, 412–415.
9. Hamani, C., Saint-Cyr, J.A., Fraser, J., Kaplitt, M., and Lozano A.M. (2004). The subthalamic nucleus in the context of movement disorders. Brain *127*, 4–20.

[1]Department of Neurology, Charité-University Medicine Berlin, CVK, Berlin, Germany. [2]Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, London, UK. [3]Department of Neurosurgery, Charité-University Medicine Berlin, CVK, Berlin, Germany. [4]Department of Neurology, Chang Gung Memorial Hospital and University, Taipei, Taiwan. [5]Department of Physiology, Anatomy and Genetics, Oxford, UK. [6]Department of Neurology and [7]Neurosurgery, University Hospitals Leuven, Leuven, Belgium. [8]Department of Neurological Surgery, Radcliffe Infirmary, Oxford, UK.
E-mail: p.brown@ion.ucl.ac.uk